204. *The Action of Acetic Anhydride on* N-*Nitrosophenylglycine and Some of its Derivatives.*

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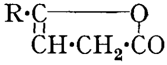
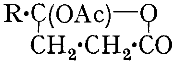
THE analogy between the nitroso-group and the carbonyl group is well recognised and has often been exemplified. The tendency of the nitroso-group to pass into the oximino-form is, however, greater than that of the carbonyl group to enolise. It should be possible to observe, in suitably chosen nitroso-compounds, ring formations which are the counterpart of those involving the enolisation of carbonyl groups.

A γ- or δ-keto-acid, under the influence of acetic anhydride, will produce either an unsaturated lactone (I) or the acetyl derivative of a hydroxy-lactone (II) (Bredt, *Annalen*, 1886, **236**, 225):



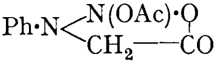
$$\begin{array}{l}\mathrm{R{\cdot}C\text{———}O}\\ \mathrm{\;\;\|\qquad\qquad |}\\ \mathrm{CH{\cdot}CH_2{\cdot}CO}\end{array}$$

(I.)



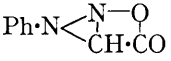
$$\begin{array}{l}\mathrm{R{\cdot}C(OAc){-}O}\\ \mathrm{CH_2{\cdot}CH_2{\cdot}CO}\end{array}$$

(II.)



$$\mathrm{Ph{\cdot}N}\!<\!\begin{array}{l}\mathrm{N(OAc){\cdot}O}\\ \mathrm{CH_2\text{——}CO}\end{array}$$

(III.)



$$\mathrm{Ph{\cdot}N}\!<\!\begin{array}{l}\mathrm{N{-}O}\\ \mathrm{CH{\cdot}CO}\end{array}$$

(IV.)

It might be expected that such a compound as *N*-nitrosophenylglycine would undergo a similar change with the formation of (III), since here the formation of a double bond is not possible.

In fact, when *N*-nitrosophenylglycine is dissolved in acetic anhydride and kept, an elimination of water takes place. The resulting crystalline *compound* is relatively stable, but may be decomposed by heating with acids or alkalis. When heated with moderately concentrated hydrochloric acid, it is broken down almost quantitatively into phenylhydrazine, formic acid, and carbon dioxide. With a hot 5% solution of caustic soda, the original nitrosophenylglycine is regenerated. A determination of the molecular weight cryoscopically in nitrobenzene gives the value 166; therefore the reaction with acetic anhydride has not involved two molecules of nitrosophenylglycine.

The above facts are best interpreted by assigning the structure (IV) to the substance. Further confirmation is furnished by the behaviour of the *N*-nitroso-derivatives of α-anilinopropionic acid and α-anilino*iso*butyric acid. The former behaves similarly to *N*-nitrosophenylglycine; the latter is recovered unchanged after the treatment with acetic anhydride. That is, the elimination of water is prevented by the presence of the *gem*-dimethyl group. The carboxylic acid group must enter into the reaction, since the *N*-nitroso-derivative of anilinoacetonitrile is unaffected by acetic anhydride.

It is intended to apply this reaction to other nitrosocarboxylic acids as opportunity offers.

EXPERIMENTAL.

N-*Nitrosophenylglycine.*—The following method is different from that recorded in the literature. Into a stirred suspension of phenylglycine (50 g.; 1 mol.) in water (600 c.c.) at 0°, a solution of sodium nitrite (25 g.; 1 mol.) in water (150 c.c.) was run during 30 minutes; solution was practically complete after 2 hours. The filtered solution was acidified with hydrochloric acid, and the precipitated *N*-nitrosophenylglycine washed with cold water and dried in air. Yield, 54·5 g. The product decomposed at 102—103° and gave a strong Liebermann nitroso-test.

Action of Acetic Anhydride on N-*Nitrosophenylglycine.*—*N*-Nitrosophenylglycine (20 g.), treated with acetic anhydride (100 g.), dissolved after 1 hour. After 24 hours, the solution was poured into water (750 c.c.) with stirring, and the precipitate collected, washed with cold water, and dried in a vacuum desiccator. Yield, 13·6 g. (73%). One recrystallisation from boiling water gave a *product* (11·8 g.), constant m. p. 134—134·5°. It did not give the Liebermann nitroso-test (Found: C, 59·3; H, 3·9; N, 17·5; *M*, cryoscopic in nitrobenzene, 166. $C_8H_6O_2N_2$ requires C, 59·3; H, 3·7; N, 17·3%; *M*, 162).

Decomposition of the Product by Hydrochloric Acid.—When a mixture of the substance (4 g.), water (40 c.c.), and concentrated hydrochloric acid (20 c.c.) was warmed in a water-bath, solution gradually took place, accompanied by a vigorous evolution of carbon dioxide. The solution was then concentrated to about 15 c.c., the distillate being collected. The concentrated solution, on cooling in ice, deposited phenylhydrazine hydrochloride (3·36 g.; 94% of the theoretical), which was identified by its m. p. (228—230°; after once recrystallising from water, 233—234°) and by conversion into benzaldehydephenylhydrazone (m. p. 157°).

Formic acid was detected in the distillate by its reaction with resorcinol and sulphuric acid (Krauss and Tampke, *Chem.-Ztg.*, 1921, **45**, 521), and by the precipitation of metallic mercury when a solution of its mercuric salt was heated (Mulliken, " The Identification of Pure Organic Compounds ").

For the quantitative determination of the amount of formic acid, the acid reaction mixture from the decomposition of 0·9561 g. of the substance was steam-distilled. The amount of formic acid in the distillate (2 l.), determined by the method of Franzen and Greve (*J. pr. Chem.*, 1909, **80**, 386), was 99·6% of the theoretical.

Decomposition of the Product by Sodium Hydroxide.—The substance (2 g.) was suspended in water (20 c.c.), and sodium hydroxide (1 g.) added. After heating on a boiling water-bath under reflux for 3 hours, cooling and filtering, the solution was made slightly acid with hydrochloric acid and placed in an ice-bath. The precipitate was filtered off, washed with cold water, and dried in air. Yield, 2·0 g. (90% of the theoretical) of a product, decomp. 98—100°, identified as *N*-nitrosophenylglycine by comparison with an authentic sample.

N-*Nitroso-α-anilinopropionic Acid.*—α-Anilinopropionic acid (15 g.; 1 mol.) (Nastvogel, *Ber.*, 1890, **23**, 2010) was suspended in water (125 c.c.), treated with concentrated hydrochloric acid (9·9 c.c.; 1 mol.), and cooled to 0°. A solution of sodium nitrite (6·3 g.; 1 mol.) in water (20 c.c.) was run in slowly with vigorous stirring. After 1 hour a dark brown, viscous oil had separated. This crystallised over-night in the ice-chest and was then filtered off, washed with water, and dried in air. Yield, 9 g. (51% of the theoretical) of a product which decomposed at 80—81° and gave a strong Liebermann nitroso-test (Found : N, 14·3. Calc. for $C_9H_{10}O_3N_2$: N, 14·4%).

Action of Acetic Anhydride on N-*Nitroso-α-anilinopropionic Acid.*—The acid (8 g.) was treated with acetic anhydride (40 g.) in the same way as described for nitrosophenylglycine. Yield, 3·25 g. (45% of the theoretical) of a product, m. p. 93—95°. Three crystallisations from aqueous alcohol raised the m. p. to 98—99°, and the purified *substance* did not give the Liebermann nitroso-test (Found : C, 61·5; H, 4·6; N, 16·0; *M*, cryoscopic in benzene, 180. $C_9H_8O_2N_2$ requires C, 61·4; H, 4·5; N, 15·9%; *M*, 176).

Decomposition of the Substance $C_9H_8O_2N_2$ *by Hydrochloric Acid.*—The substance (0·5 g.) was decomposed in the same way as the corresponding derivative of phenylglycine. Phenylhydrazine hydrochloride (0·33 g.) was isolated and identified, and carbon dioxide was generated during the decomposition. Acetic acid was identified in the aqueous distillate by conversion into calcium acetate, the destructive distillation of which gave acetone (*p*-bromophenylhydrazone, m. p. and mixed m. p. 88°).

Decomposition of the Substance $C_9H_8O_2N_2$ *by Sodium Hydroxide.*—The substance (0·5 g.) was treated in the same way as the corresponding derivative of phenylglycine. *N*-Nitroso-α-anilinopropionic acid (0·16 g.; 29% of the theoretical) was recovered and identified.

α-*Anilino*iso*butyric Acid.*—α-Anilino*iso*butyronitrile was prepared and converted into the amide (von Walther and Hübner, *J. pr. Chem.*, 1916, **93**, 126), which was hydrolysed by hydrochloric acid to the free acid. This procedure gave a better yield (86% of the theoretical) than direct hydrolysis of the nitrile.

*Nitroso-α-anilino*iso*butyric Acid.*—A mixture of anilino*iso*butyric acid (5 g.), water (100 c.c.), and concentrated hydrochloric acid (3 c.c.) at 0° was slowly treated with a solution of sodium nitrite (2·0 g.) in water (50 c.c.). After a short time the precipitated nitroso-compound was filtered off and dried in air. Yield, 5·1 g. (73% of theoretical) of a product decomposing sharply at 117°. After recrystallisation from aqueous alcohol the decomposition point was unaltered. The substance gave the Liebermann nitroso-test (Found : N, 13·6, 13·7. Calc. for $C_{10}H_{12}O_3N_2$: N, 13·5%).

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